



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|------------------------|---------------------|------------------|
| 10/007,275 | 10/26/2001 | Timo Kars van den Berg | 080743-235-001 | 5284 |

7590

12/03/2003

Ronald A. Sandler
Jones, Day, Reavis & Pogue
77 West Wacker Drive
Chicago, IL 60540

| |
|----------|
| EXAMINER |
|----------|

YAEN, CHRISTOPHER H

| | |
|----------|--------------|
| ART UNIT | PAPER NUMBER |
|----------|--------------|

1642

DATE MAILED: 12/03/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/007,275

Applicant(s)

BERG ET AL.

Examiner

Christopher H Yaen

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 June 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-8 and 11-14 is/are pending in the application.
- 4a) Of the above claim(s) 11-14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 3-8 is/are rejected.
- 7) ☒ Claim(s) 1 and 3-8 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other:

DETAILED ACTION

1. The amendment filed June 30, 2003 (paper no. 8) is acknowledged and entered into the record. Accordingly, claims 2, 9-10 are cancelled without prejudice or disclaimer, claims 11-14 are withdrawn from further prosecution as being drawn to a non-elected invention.
2. This application contains claim 11-14 drawn to an invention nonelected without traverse in Paper No. 5. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.
3. Claims 1, 3-8 are examined on the merits.

Claim Objections

4. Claims 1, and 3-8 are objected to because of the following informalities: claims recite "microphages" and "macrophases", both of which are not supported by the specification. It is assumed that the applicant intends to recite "macrophages". Appropriate correction is required.

Claim Rejections Maintained - 35 USC § 112, 1st paragraph

5. The rejection of claims 8 under 35 USC 112, 1st paragraph as lacking enablement is maintained for the reasons of record. Applicant argues that the specification and a prior art reference fully disclose the specifically recited antibodies and further states that a deposit of the claimed antibodies are not needed. Applicant arguments have been carefully considered but are not found persuasive because it

Art Unit: 1642

appears that the specific method of inhibiting cell function is dependent on the use of the specifically disclosed antibodies and as such would appear to be critical to the functionality of the instant invention. Without such antibodies, the skilled artisan would be forced into undue experimentation to practice the claimed invention. Furthermore, it does not appear that the claimed antibodies are readily available to the skilled artisan in a form that can be reproduced or purchased.

Claim Rejections Maintained - 35 USC § 112, 1st paragraph

6. The rejection of claims 1, and 3-8 under 35 USC 112, 1st paragraph as lacking enablement is maintained for the reasons of record. Applicant argues that “[g]enerally, it is not necessary for a drug to be effective that all type of cellular functions be inhibited.” It is also argues that relevant cellular functions associated with the diseases concerned have been disclosed in the specification, wherein the use of Fab fragments are illustrative examples of claimed inhibitory functionality. Applicant also argues the transition from in-vitro to in-vivo usage is within acceptable experimentation. Applicant's arguments have been carefully considered but are not found persuasive.

The specification must be commensurate in scope to what is claimed. The specification teaches TWO specific Fab fragments that show inhibitory function in vitro. As stated in the prior office action, the specification teaches that not all whole antibodies are effective in eliciting the desired functionality but rather induced an effect counter to that which is being claimed. Such effects underscores the importance to the modifications made to the Fab fragment antibodies claimed, and as such not all substances, as

Art Unit: 1642

claimed, are effective in inhibiting cellular function. Furthermore, the experimentation involved in turning an in-vitro product/result into a predictive/effective in-vivo product/result is not within the acceptable realm of experimentation because the diseases claimed (i.e cancer and immune modulation) are both considered rather unpredictable diseases. There is insufficient guidance and objective evidence that the teachings of the specification are indicative of anti-inflammatory or anti-cancer behavior in-vivo, i.e. in an individual; wherein it would not be predictable to one of skill in the art to use the method in order to inhibit anti-inflammatory or anti-cancer behavior in any individual. Those of skill in the art recognize that in vitro assays and or cell-cultured based assays are generally useful to observe basic physiological and cellular phenomenon such as screening the effects of potential drugs. However, clinical correlations are generally lacking. The greatly increased complexity of the in vivo environment as compared to the very narrowly defined and controlled conditions of an in-vitro assay does not permit a single extrapolation of in vitro assays to human diagnostic efficacy with any reasonable degree of predictability. In vitro assays cannot easily assess cell-cell interactions that may be important in a particular pathological state. Furthermore it is well known in the art that cultured cells, over a period time, lose phenotypic characteristics associated with their normal counterpart cell type.

Freshney (Culture of Animal Cells, A Manual of Basic Technique, Alan R. Liss, Inc., 1983, New York, p4) teach that it is recognized in the art that there are many differences between cultured cells and their counterparts *in vivo*. These differences stem from the dissociation of cells from a three-dimensional geometry and their

Art Unit: 1642

propagation on a two-dimensional substrate. Specific cell interactions characteristic of histology of the tissue are lost. The culture environment lacks the input of the nervous and endocrine systems involved in homeostatic regulation *in vivo*. Without this control, cellular metabolism may be more constant *in vitro* but may not be truly representative of the tissue from which the cells were derived. This has often led to tissue culture being regarded in a rather skeptical light (p. 4, see Major Differences *In Vitro*). Further, although drawn specifically to cancer cells, Dermer (Bio/Technology, 1994, 12:320) teaches that, "petri dish cancer" is a poor representation of malignancy, with characteristics profoundly different from the human disease. Further, Dermer teaches that when a normal or malignant body cell adapts to immortal life in culture, it takes an evolutionary type step that enables the new line to thrive in its artificial environment. This step transforms a cell from one that is stable and differentiated to one that is not. Yet normal or malignant cells *in vivo* are not like that. The reference states that evidence of the contradictions between life on the bottom of a lab dish and in the body has been in the scientific literature for more than 30 years.

Clearly it is well known in the art that cells in culture exhibit characteristics different from those *in vivo* and cannot duplicate the complex conditions of the *in vivo* environment involved in host-tumor and cell-cell interactions. Therefore, the data presented in the instant specification is not predictive nor commensurate in scope to the claims of inhibiting cellular function *in vivo*.

Conclusion

7. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.


Application/Control Number: 10/007,275

Page 7

Art Unit: 1642

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
November 3, 2003


ANTHONY C. CAPUTO
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1000